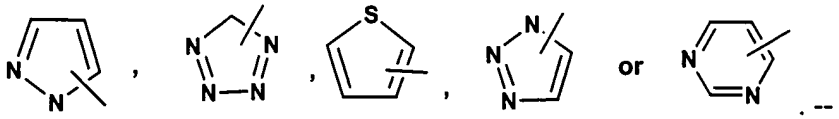
cycloheteroalkoxy, or cycloheteroalkylalkoxy); and may be optionally independently substituted with from one to five substituents, which may be the same or different;

including pharmaceutically acceptable salts thereof, prodrugs thereof, and all stereoisomers thereof. --

--71. (Amended) The compound as defined in Claim 64 wherein R^1 is



. --

REMARKS

Claims 1 to 3, 6, 8 to 10, 14, 15, 17, 19, 20, 22, 24 to 31 and new Claims 63 to 74 are present for purposes of prosecution.

Reconsideration of the rejection of this application is respectfully requested in view of the above amendments and the following remarks.

In response to the final Official Action of March 7, 2002, an Amendment filed April 9, 2002 was not entered because the Examiner decided in the Advisory Action mailed May 7, 2002 that the proposed amendments set out therein did not place the application in better form for appeal. The Examiner pointed out that some of the claims still encompassed R^1 as imidazole which is disclosed in Jegham et al. U.S. 5,434,169. The present Preliminary Amendment is essentially the same as the April 9, 2002 Amendment except that the claims have been amended to delete imidazole from R^1.

It is respectfully requested that this Preliminary Amendment be entered in place of the Amendment of April 9, 2002.

In the final Official Action of March 7, 2002, Claim 1 is rejected under 35 USC 112, first paragraph in view of the provisos included in the previously amended Claim 1.

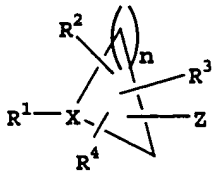
All provisos have been removed from Claims 1 and 64.

Claim 14 and claims dependent thereon are rejected on use of the zig zag symbol. The zig zag symbols have been replaced with the Z group as shown in Claim 1.

In view of the above, it is believed that all formal objections have been overcome.

Claim 1 and Claim 64 have been amended to include heteroaryl rings (for R^1) as set out on page 18 of the specification and the group  set out in Claim 19.

Applicants' invention as claimed in Claim 1 is directed to a compound having the structure

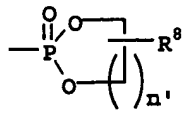


wherein n is 4;

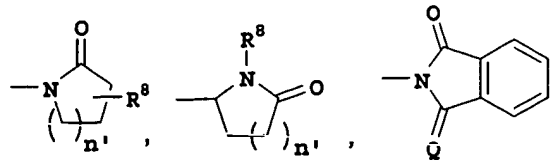
X is N;

Z is a heteroaryl group;

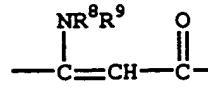
R^1 is alkynyl, alkoxy, alkenyloxy, alkynyloxy, (alkyl or aryl)$_3$Si (where each alkyl or aryl group is independent), cycloalkenyl, amino, alkylamino, dialkylamino, alkenylamino, alkynylamino, arylalkylamino, cycloheteroalkyl, cycloheteroalkylalkyl, heteroaryl, heteroarylamino, heteroaryloxy, arylsulfinyl, arylsulfonyl, thio, alkylthio, alkylsulfinyl, alkylsulfonyl, heteroarylthio, heteroarylsulfinyl, heteroarylsulfonyl, halogen, haloalkyl, polyhaloalkyl, polyhaloalkoxy, aminothio, aminosulfinyl, aminosulfonyl, alkylsulfonylamino, alkenylsulfonylamino, alkynylsulfonylamino, arylsulfonylamino, heteroarylsulfonylamino, heteroarylaminocarbonyl, hydroxy, acyl, carboxy, alkylcarbonylamino, arylcarbonyloxy, arylcarbonylamino, heteroarylcarbonyloxy, heteroarylcarbonylamino, cyano, nitro, alkenylcarbonylamino, alkynylcarbonylamino, alkylaminocarbonylamino, alkenylaminocarbonylamino, alkynylaminocarbonylamino, arylaminocarbonylamino, heteroarylaminocarbonylamino, alkoxycarbonylamino, alkenyloxycarbonylamino, alkynyloxycarbonylamino, aryloxycarbonylamino, heteroaryloxycarbonylamino, aminocarbonylamino, alkylaminocarbonyloxy, alkoxycarbonylamino, l,l-(alkoxyl or aryloxy)$_2$alkyl (where the two aryl or alkyl substituents can be independently defined, or linked to one another to form a ring), $S(O)_2R^6R^7$, $-NR^6(C=NR^7)$alkyl, $-NR^6(C=NR^7)$alkenyl, $-NR^6(C=NR^7)$alkynyl, $-NR^6(C=NR^7)$heteroaryl, $-NR^8(C=NCN)$-amino,



pyridine-N-oxide,



(where Q is O or H_2 and n' is 0, 1, 2 or 3) or

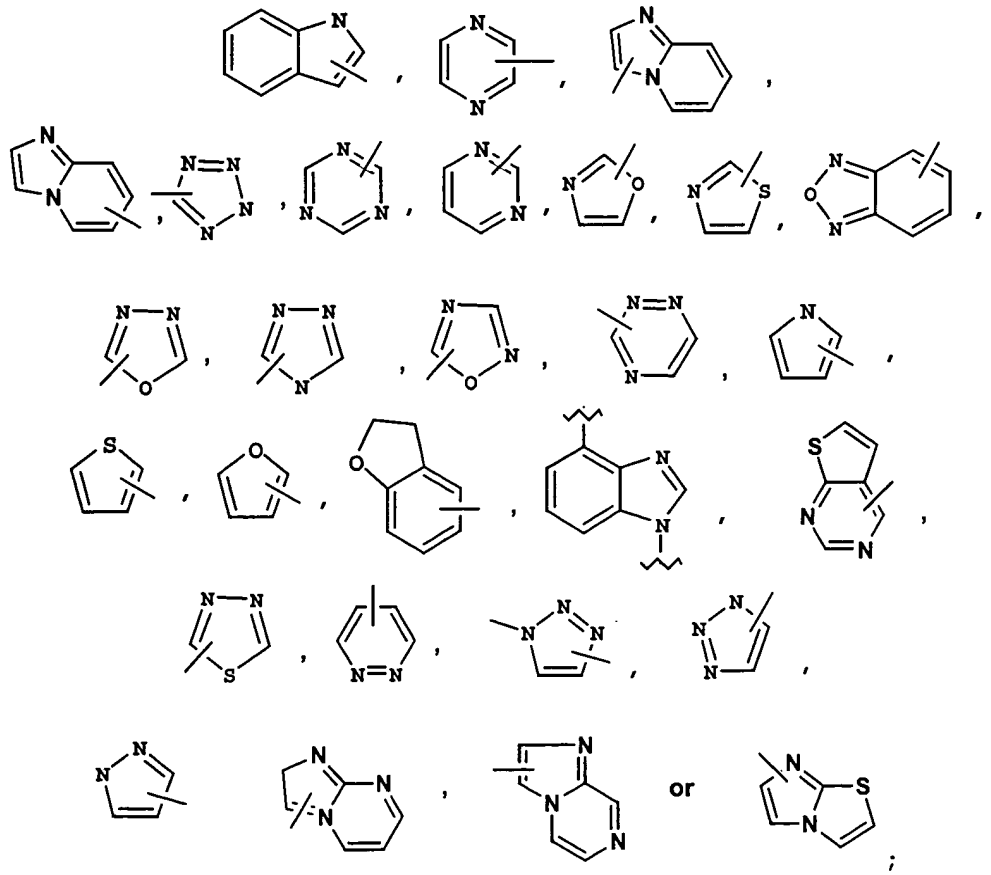


; -PO(R^{13})(R^{14}), (where R^{13} and R^{14} are independently alkyl, aryl, alkoxy, aryloxy, heteroaryl, heteroarylalkyl, heteroaryloxy, heteroarylalkoxy, cycloheteroalkyl, cycloheteroalkylalkyl, cycloheteroalkoxy, or cycloheteroalkylalkoxy);

R^6, R^7, R^8, R^{8a} and R^9 are the same or different and are independently hydrogen, alkyl, haloalkyl, aryl, heteroaryl, arylalkyl, cycloalkyl, (cycloalkyl)alkyl, or cycloheteroalkyl;

and R^1 may be unsubstituted or substituted with from one to five substituents;

and wherein the R^1 heteroaryl group is selected from



;

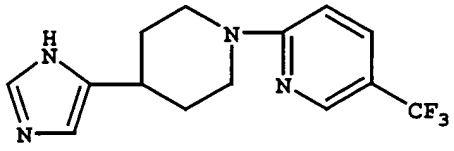
R^2, R^3 and R^4 are the same or different and are independently any of the groups originally set out for R^1 and may be optionally independently substituted with from one to five substituents, which may be the same or different;

including pharmaceutically acceptable salts thereof, prodrugs thereof, and all stereoisomers thereof.

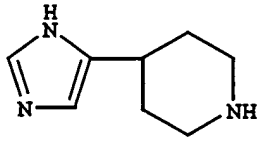
It is submitted that Applicants' invention as now claimed is patentable over all cited references each taken alone or in any combination.

In the March 7, 2002 final Official Action, Claims 1-4, 6-10, 12, 13, 15-19, 22, 24, 25, 31, and Claims 64-70 are rejected under 35 U.S.C. 102(b) as being anticipated by Ganellin et al, Chem Abstract 123:198692, in that "pyridine anticipates heteroaryl".

Ganellin et al disclose compounds of the structure



and



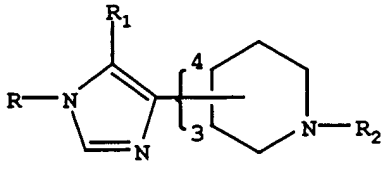
As indicated by the Examiner, Ganelli et al disclose compounds where "the corresponding R^1 is pyridine and Z is imidazole."

Claim 1 has been amended so that pyridyl and H are no longer encompassed by R^1.

In view of the foregoing, it is submitted that Claims 1, 3, 6, 8 to 10, 14, 15, 17, 19, 22, 24, 25 and 31 and Claim 64 are patentable over Ganellin et al.

Claims 1, 2, 4, 6-10, 12, 14-16, 22, 24, 25 and 31 are rejected under 35 U.S.C. 102(b) as being anticipated by Arrang et al (US Patent 4,707,487) and also under 35 USC 103(a). The Examiner contends that Arrang reads on R^1 as aminocarbonyl.

U.S. Patent No. 4,707,487 to Arrang et al discloses (4-imidazolyl)-piperidines of the formula

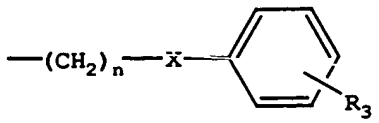


in which

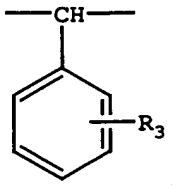
R_1 denotes a hydrogen atom or a methyl or ethyl group,

R denotes a hydrogen atom or a radical R_2, and

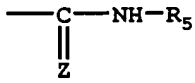
R_2 denotes a linear or branched alkyl group having 1 to 6 carbon atoms; a piperonyl group; a 3-(1-benzimidazolonyl)propyl group; a group of formula



in which n is 0, 1, 2 or 3, X is a single bond or alternatively -O-, -S-, -NH-, -CO-, -CH=CH- or



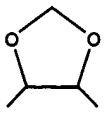
and R_3 is H, CH_3, halogen, CN, CF_3 or an acyl group -COR_4, R_4 being a linear or branched alkyl group having 1 to 6 carbon atoms, a cycloalkyl group having 3 to 6 carbon atoms or a phenyl group which can bear a CH_3 or F substituent; or alternatively a group of formula



in which Z denotes an O or S atom or a divalent group NH, N-CH_3 or N-CN and R_5 denotes a linear or branched alkyl group having 1 to 8 carbon atoms, a cycloalkyl group having 3 to 6 carbon atoms which can bear a phenyl substituent, a cycloalkyl (3 to 6 C) alkyl (1 to 3 C, linear or branched) group, a phenyl group which can bear a CH_3, halogen or CF_3 substituent, a phenylalkyl (1 to 3 C, linear or branched) group or a naphthyl, adamantyl or p-toluenesulphonyl group, as well as the pharmaceutically acceptable salts thereof.

R_2 in the Arrang et al compounds (correspond to Applicants' R^1 group) includes

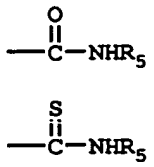
(1) alkyl

(2) piperonyl (a phenylmethyl group having a  fused to the phenyl group -- thus piperonyl is an arylalkyl group)

(3) 3-(1-benzimidazolonyl)propyl (that is, a cycloheteroalkyl group)

(4) (a) phenyl
(b) phenylalkyl
(c) phenyl-X- (where X is a bond, O, S, NH, CO, -CH=CH- or phenylmethylene)
(d) phenyl-X-alkyl

(5) acyl (COR_4- where R_4 is alkyl,cycloalkyl or phenyl

(6) 

where R_5 is alkyl, cycloalkyl, cycloalkylalkyl, phenyl, naphthyl, adamantyl or p-toluenesulfonyl.

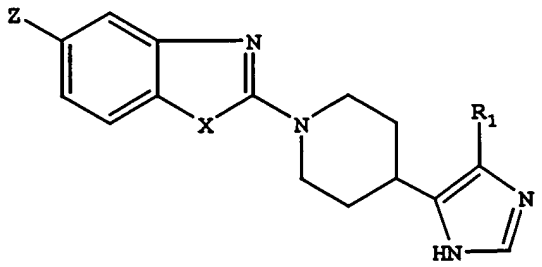
Claim 1 has been amended to delete from the definition of R^1 the term aminocarbonyl.

Thus, the amended definition of R^1 no longer encompasses any of the R_2 groups of Arrang et al.

In view of the foregoing, it is submitted that Applicants' compounds as claimed in Claims 1, 2, 6, 8 to 10, 14-16, 22, 24, 25, 31 and Claim 64 are patentable over Arrang et al.

Claims 1-4, 6-10, 12, 13, 15-18, 22, 24, 25 and 31 are rejected under 35 U.S.C. 102(b) as being anticipated by Jegham et al (US Patent 5,280,030) and also under 35 USC 103(a). The Examiner contends that this reference discloses a bicyclic ring which anticipates heteroaryl.

Jegham et al disclose a piperidine derivative of formula (I)



in which R_1 represents a hydrogen atom, a linear or branched (C_{1-6})alkyl group or a cyclo(C_{3-8})alkyl group, X represents an oxygen atom, a sulphur atom or a group of general formula N-R_3 in which R_3 is a hydrogen atom, or a linear or branched (C_{1-8})alkyl, cyclo(C_{3-6})alkyl, cyclo(C_{3-6})alkylmethyl, (C_{1-4})alkoxy-(C_{1-4})alkyl, phenyl, pyridin-4-yl, pyridin-3-yl, pyridin-4-ylmethyl or pyridin-3-ylmethyl group and Z represents a hydrogen or fluorine atom and acid addition salts thereof with pharmaceutically acceptable acids.

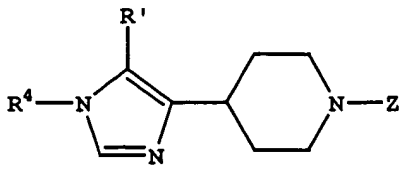
Thus, the Jegham et al bicyclic group linked to the N of the piperidine includes a benzimidazole, a benzthiazole or a benzoxazole.

Please note that Claim 1 has been amended so that the R^1 group no longer includes a benzimidazole, a benzthiazole or a benzoxazole.

In view of the foregoing, it is submitted that Claims 1 to 3, 6, 8 to 10, 12-13, 15-18, 22, 24, 25, 31 and Claims 64-70 are patentable over Jegham et al (5,280,030).

Claims 1, 2, 4, 6, 8-10, 12, 14, 16, 22, 24, 25 and 31 are rejected under 35 U.S.C. 102(b) as being anticipated by Durant et al (US Patent 5,663,350) and also under 35 USC 103(a). The Examiner contends that Durant teaches that R^2 can be piperonyl.

Durant et al disclose compounds of the structure



wherein Z is

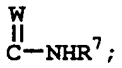
or R^2;

R' is H or C_1-C_4 alkyl;

R^1 is OR^2, $(CH_2)_nR^3$, C_1-C_{20} alkyl, C_1-C_{20} alkenyl, C_1-C_{20} cycloalkyl, C_1-C_{20} cycloalkenyl and C_1-C_{20} alkylaryl;

R^2 is C_1-C_6 alkyl, piperonyl or $(CH_2)_nR^3$;

R^3 is adamantyl methyl, C_1-C_{20} cycloalkyl, C_1-C_{20} cycloalkyl phenyl methylene, C_1-C_{20} dicycloakyl methylene, diphenyl methylene, Y-C_6H_4-R^5



R^4 is H,

or C_1-C_4 alkyl;

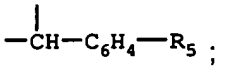
R^5 is H, CH_3, halogen, CN, CF_3 or COR^6;

R^6 is C_1-C_{20} linear or branched chain alkyl, C_1-C_{20} cycloalkyl, phenyl or phenyl substituted with 1-3 substituents selected from the group consisting of CH_3 or F;

R^7 is C_1-C_{20} linear or branched chain alkyl, C_1-C_{20} cycloalkyl phenyl methylene, C_1-C_{20} cycloalkyl alkyl methylene, C_1-C_{20} dicycloalkyl methylene, phenyl, phenyl substituted with 1-3 substituents selected from the group consisting of CH_3, halogen, C_1-C_3 alkyl (linear or branched);

X is S or O;

Y is a single bond or alternatively -O-, -S-, -NH-, -CO-, -CH=CH- or



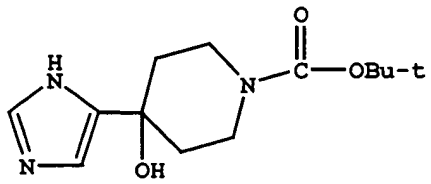
W is O, S, NH, NCH_3 or NCN; and n=0-10.

Applicants' Claim 1 has been amended so that R^1 no longer includes piperonyl.

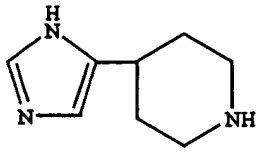
In view of the above amendments to the definition of R^1, it is submitted that Applicants' compounds as claimed in Claims 1 to 3, 6, 8 to 10, 14, 22, 24, 25, 31 and Claims 64-70 are patentable over Durant et al.

Claims 1, 2, 4, 6,10, 12, 14-16, 22, 24, 25 and 31 are rejected under 35 U.S.C. 102(b) as being anticipated by Lange et al, Chem Abstract 124:965601. The Examiner contends that Lange et al teach a carboxy group attached to the N of the piperidine ring.

Lange et al disclose compounds of the structure



and

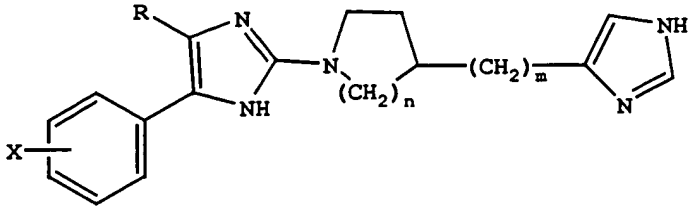


Claim 1 has been amended to delete alkylcarbonyloxy from the definition of R^1.

In view of the above amendments to the definition of R^1, it is submitted that Applicants' compounds as claimed in Claims 1, 2, 6, 8 to 10, 14, 15, 22, 24, 25 and 31 and Claim 64 are patentable over Lange et al.

Claims 1-3, 6, 8-10, 14, 15, 17, 19, 20, 22, 24-27, 31, and 64-74 are rejected under 35 USC 102(b) as being anticipated by Jegham et al and also under 35 USC 103(a).

Jegham et al disclose compounds of the structure



(I)

where R represents a hydrogen atom or a phenyl group optionally substituted by a halogen atom or a methyl, methoxy, trifluoromethyl or nitro group; X represents a hydrogen or halogen atom or a methyl, methoxy, trifluoromethyl or nitro group; n is equal to 1 or 2, and m is equal to 0 or 1.

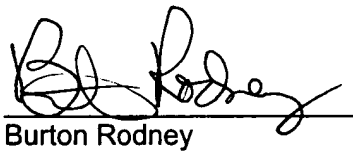
Applicants have amended Claim 1 and Claim 64 so that R^1 includes specific heteroaryl groups none of which includes the 2-imidazolyl present in Jegham et al.

Accordingly, it is submitted Jegham et al does not disclose or suggest Applicants' compounds as now claimed. Thus, it is believed that Claims 1 to 3, 6, 8 to 10, 14, 15, 17, 19, 20, 22, 24 to 27, 31, and 64 to 74 are patentable over Jegham et al.

In view of the foregoing, it is submitted that Claims 1 to 3, 6, 8 to 10, 14, 15, 17, 19, 20, 22, 24 to 31 and Claims 63 to 74 overcome all formal objections and are patentable over all cited prior art. Accordingly, it is believed that the above claims are in condition of allowance.

Applicants note with appreciation that Claims 28 to 30 and 63 are allowable.

Respectfully submitted,



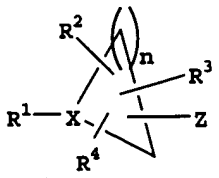
Burton Rodney
Attorney for Applicants
Reg. No. 22,076

Bristol-Myers Squibb Company
Patent Department
P.O. Box 4000
Princeton, NJ 08543-4000
(609) 252-4336

Date: Aug 6, 2002

MARKED-UP VERSION OF AMENDED CLAIMS

--1. (Twice Amended) A compound having the structure

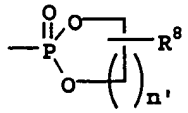


wherein n is 4;

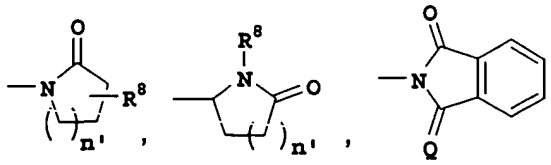
X is N;

Z is a heteroaryl group;

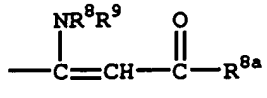
R^1 is alkynyl, alkoxy, alkenyloxy, alkynyloxy, (alkyl or aryl)$_3$Si (where each alkyl or aryl group is independent), cycloalkenyl, amino, alkylamino, dialkylamino, alkenylamino, alkynylamino, arylalkylamino, cycloheteroalkyl, cycloheteroalkylalkyl, heteroaryl, heteroarylamino, heteroaryloxy, arylsulfinyl, arylsulfonyl, thio, alkylthio, alkylsulfinyl, alkylsulfonyl, heteroarylthio, heteroarylsulfinyl, heteroarylsulfonyl, halogen, haloalkyl, polyhaloalkyl, polyhaloalkoxy, aminothio, aminosulfinyl, aminosulfonyl, alkylsulfonylamino, alkenylsulfonylamino, alkynylsulfonylamino, arylsulfonylamino, heteroarylsulfonylamino, heteroarylaminocarbonyl, hydroxy, acyl, carboxy, [aminocarbonyl,] [alkylcarbonyloxy,] alkylcarbonylamino, arylcarbonyloxy, arylcarbonylamino, heteroarylcarbonyloxy, heteroarylcarbonylamino, cyano, nitro, alkenylcarbonylamino, alkynylcarbonylamino, alkylaminocarbonylamino, alkenylaminocarbonylamino, alkynylaminocarbonylamino, arylaminocarbonylamino, heteroarylaminocarbonylamino, alkoxycarbonylamino, alkenyloxycarbonylamino, alkynyloxycarbonylamino, aryloxycarbonylamino, heteroaryloxycarbonylamino, aminocarbonylamino, alkylaminocarbonyloxy, alkoxycarbonylamino, l,l-(alkoxyl or aryloxy)$_2$alkyl (where the two aryl or alkyl substituents can be independently defined, or linked to one another to form a ring), S(O)$_2$$R^6$$R^7$, -N$R^6$(C=N$R^7$)alkyl, -N$R^6$(C=N$R^7$)alkenyl, -N$R^6$(C=N$R^7$)alkynyl, -N$R^6$(C=N$R^7$)heteroaryl, -N$R^8$(C=NCN)-amino,



pyridine-N-oxide,



(where Q is O or H_2 and n' is 0, 1, 2 or 3) or

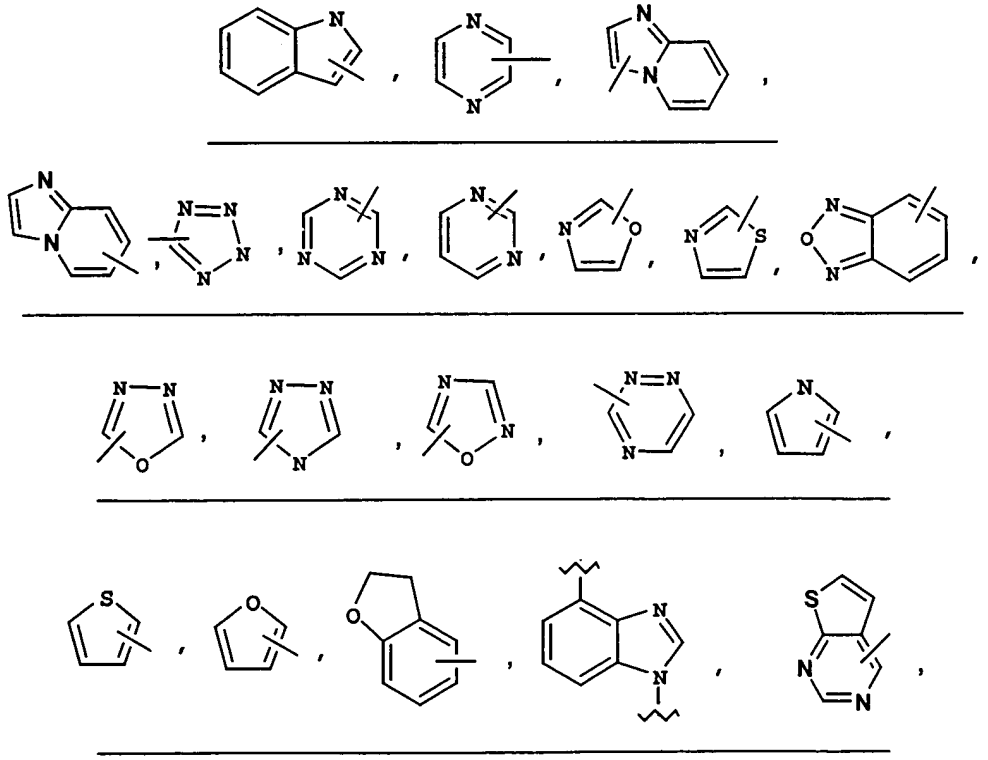


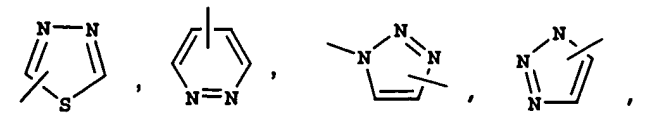
; [tetrazolyl, pyrazolyl, thiazolyl, pyrimidinyl, imidazole, oxazole, or triazole,] -PO(R^{13})(R^{14}), (where R^{13} and R^{14} are independently alkyl, aryl, alkoxy, aryloxy, heteroaryl, heteroarylalkyl, heteroaryloxy, heteroarylalkoxy, cycloheteroalkyl, cycloheteroalkylalkyl, cycloheteroalkoxy, or cycloheteroalkylalkoxy);

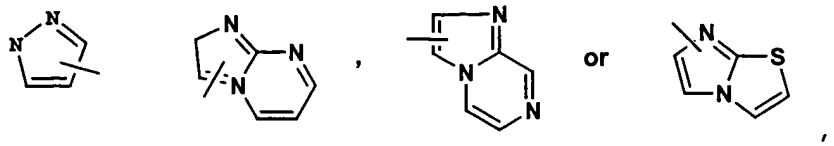
R^6, R^7, R^8, R^{8a} and R^9 are the same or different and are independently hydrogen, alkyl, haloalkyl, aryl, heteroaryl, arylalkyl, cycloalkyl, (cycloalkyl)alkyl, or cycloheteroalkyl;

and R^1 may be unsubstituted or substituted with from one to five substituents;

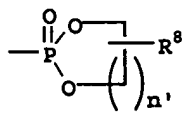
and wherein the R^1 heteroaryl group is selected from



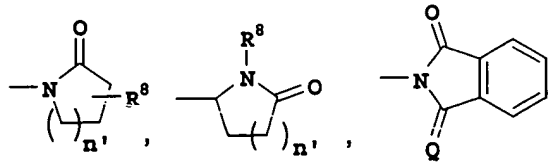




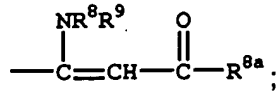
R^2, R^3 and R^4 are the same or different and are independently H, alkyl, alkenyl, alkynyl, alkoxy, alkenyloxy, alkynyloxy, (alkyl or aryl)$_3$Si (where each alkyl or aryl group is independent), cycloalkyl, cycloalkenyl, amino, alkylamino, dialkylamino, alkenylamino, alkynylamino, arylalkylamino, aryl, arylalkyl, arylamino, aryloxy, cycloheteroalkyl, cycloheteroalkylalkyl, heteroaryl, heteroarylamino, heteroaryloxy, arylthio, arylsulfinyl, arylsulfonyl, thio, alkylthio, alkylsulfinyl, alkylsulfonyl, heteroarylthio, heteroarylsulfinyl, heteroarylsulfonyl, halogen, haloalkyl, polyhaloalkyl, polyhaloalkoxy, aminothio, aminosulfinyl, aminosulfonyl, alkylsulfonylamino, alkenylsulfonylamino, alkynylsulfonylamino, arylsulfonylamino, heteroarylsulfonylamino, alkylaminocarbonyl, arylaminocarbonyl, heteroarylaminocarbonyl, hydroxy, acyl, carboxy, aminocarbonyl, alkylcarbonyl, alkoxycarbonyl, alkylcarbonyloxy, alkylcarbonylamino, arylcarbonyl, arylcarbonyloxy, arylcarbonylamino, heteroarylcarbonyl, heteroarylcarbonyloxy, heteroarylcarbonylamino, cyano, nitro, alkenylcarbonylamino, alkynylcarbonylamino, alkylaminocarbonylamino, alkenylaminocarbonylamino, alkynylaminocarbonylamino, arylaminocarbonylamino, heteroarylaminocarbonylamino, alkoxycarbonylamino, alkenyloxycarbonylamino, alkynyloxycarbonylamino, aryloxycarbonylamino, heteroaryloxycarbonylamino, aminocarbonylamino, alkylaminocarbonyloxy, alkoxycarbonylamino, l,l-(alkoxyl or aryloxy)$_2$alkyl (where the two aryl or alkyl substituents can be independently defined, or linked to one another to form a ring), S(O)$_2$R^{6}R^7, -NR^6(C=NR^7)alkyl, -NR^6(C=NR^7)alkenyl, -NR^6(C=NR^7)alkynyl, -NR^6(C=NR^7)heteroaryl, -NR^8(C=NCN)-amino,



pyridine-N-oxide,



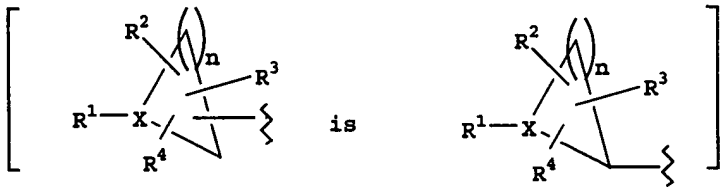
(where Q is O or H_2 and n' is 0, 1, 2 or 3) or



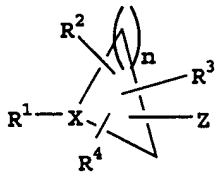
; tetrazolyl, pyrazolyl, pyridyl, thiazolyl, pyrimidinyl, imidazole, oxazole, or triazole, -PO(R^{13})(R^{14}), (where R^{13} and R^{14} are independently alkyl, aryl, alkoxy, aryloxy, heteroaryl, heteroarylalkyl, heteroaryloxy, heteroarylalkoxy, cycloheteroalkyl, cycloheteroalkylalkyl, cycloheteroalkoxy, or cycloheteroalkylalkoxy); and may be optionally independently substituted with from one to five substituents, which may be the same or different;

including pharmaceutically acceptable salts thereof, prodrugs thereof, and all stereoisomers thereof[; with the provisos that (1) where Z is imidazol-4-yl or 5-alkylimidazol-4-yl or 5-cycloalkylimidazol-4-yl, then R^1 cannot be or include a benzoxazole, benzthiazole, or benzimidazole and (2) R^1 is exclusive of 3-(1-benzimidazolonyl)-propyl]. --

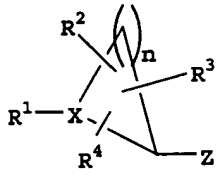
--14. (Amended) The compound as defined in Claim I wherein the moiety



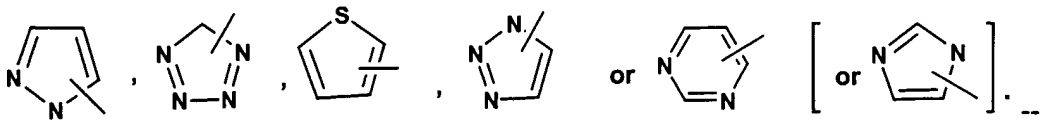
is



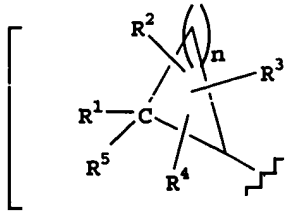
is



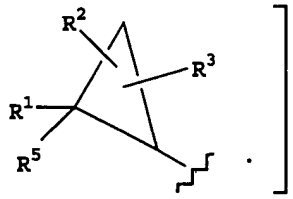
--19. (Twice Amended) The compound as defined in Claim I wherein R^1 is

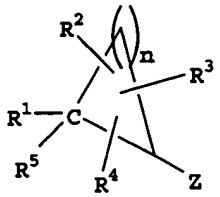


--21. (Amended) The compounds as defined in Claim 11 wherein

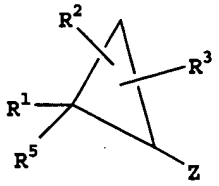


is



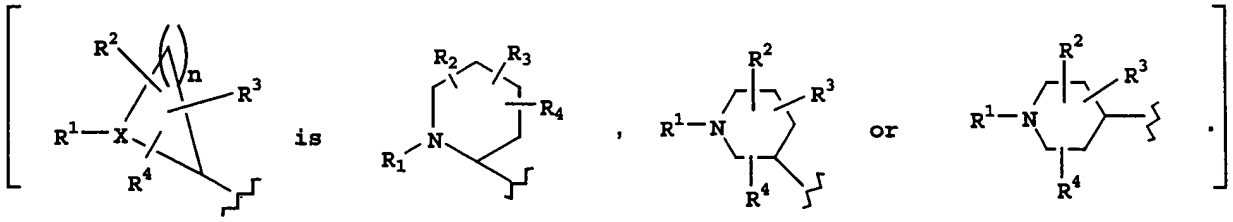


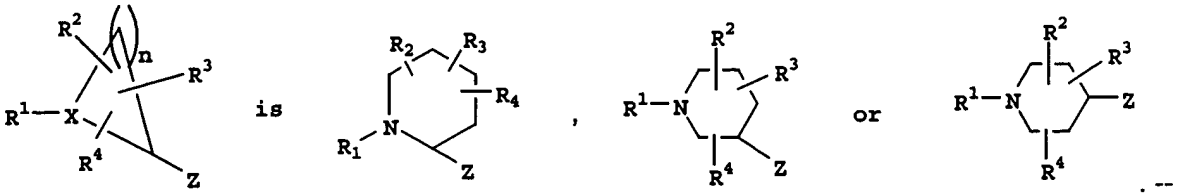
is



.--

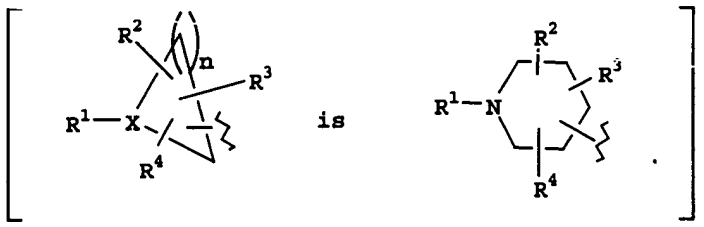
--22. (Twice Amended) The compound as defined in Claim 14 wherein

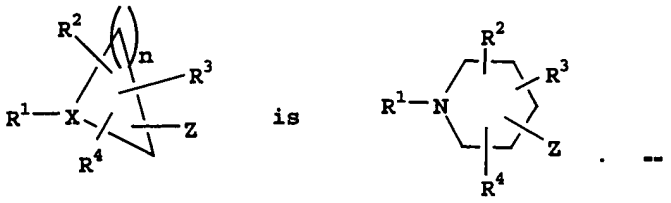




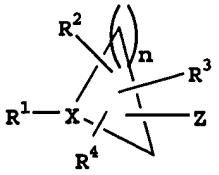
.--

--24. (Twice Amended) The compound as defined in Claim 14 wherein





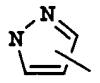
--64. (Amended) A compound having the structure



wherein n is 4;

X is N;

Z is a heteroaryl group;

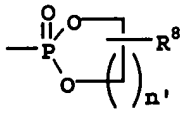
R^1 is [heteroaryl] tetrazolyl, pyrazolyl, thiazolyl, pyrimidinyl, [imidazole,]  , oxazole, or triazole;

R^6, R^7, R^8, R^{8a} and R^9 are the same or different and are independently hydrogen, alkyl, haloalkyl, aryl, heteroaryl, arylalkyl, cycloalkyl, (cycloalkyl)alkyl, or cycloheteroalkyl;

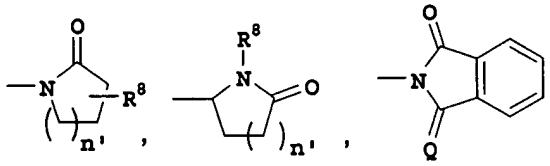
and R^1 may be unsubstituted or substituted with from one to five substituents;

R^2, R^3 and R^4 are the same or different and are independently H, alkyl, alkenyl, alkynyl, alkoxy, alkenyloxy, alkynyloxy, (alkyl or aryl)$_3$Si (where each alkyl or aryl group is independent), cycloalkyl, cycloalkenyl, amino, alkylamino, dialkylamino, alkenylamino, alkynylamino, arylalkylamino, aryl, arylalkyl, arylamino, aryloxy, cycloheteroalkyl, cycloheteroalkylalkyl, heteroaryl, heteroarylamino, heteroaryloxy, arylthio, arylsulfinyl, arylsulfonyl, thio, alkylthio, alkylsulfinyl, alkylsulfonyl, heteroarylthio, heteroarylsulfinyl, heteroarylsulfonyl, halogen, haloalkyl, polyhaloalkyl,

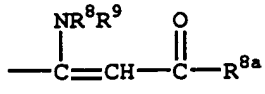
polyhaloalkoxy, aminothio, aminosulfinyl, aminosulfonyl, alkylsulfonylamino, alkenylsulfonylamino, alkynylsulfonylamino, arylsulfonylamino, heteroarylsulfonylamino, alkylaminocarbonyl, arylaminocarbonyl, heteroarylaminocarbonyl, hydroxy, acyl, carboxy, aminocarbonyl, alkylcarbonyl, alkoxycarbonyl, alkylcarbonyloxy, alkylcarbonylamino, arylcarbonyl, arylcarbonyloxy, arylcarbonylamino, heteroarylcarbonyl, heteroarylcarbonyloxy, heteroarylcarbonylamino, cyano, nitro, alkenylcarbonylamino, alkynylcarbonylamino, alkylaminocarbonylamino, alkenylaminocarbonylamino, alkynylaminocarbonylamino, arylaminocarbonylamino, heteroarylaminocarbonylamino, alkoxycarbonylamino, alkenyloxycarbonylamino, alkynyloxycarbonylamino, aryloxycarbonylamino, heteroaryloxycarbonylamino, aminocarbonylamino, alkylaminocarbonyloxy, alkoxycarbonylamino, l,l-(alkoxyl or aryloxy)$_2$alkyl (where the two aryl or alkyl substituents can be independently defined, or linked to one another to form a ring), $S(O)_2R^6R^7$, $-NR^6(C=NR^7)$alkyl, $-NR^6(C=NR^7)$alkenyl, $-NR^6(C=NR^7)$alkynyl, $-NR^6(C=NR^7)$heteroaryl, $-NR^8(C=NCN)$-amino,



pyridine-N-oxide,



(where Q is O or H_2 and n' is 0, 1, 2 or 3) or



; tetrazolyl, pyrazolyl, pyridyl, thiazolyl, pyrimidinyl, imidazole, oxazole, or triazole, $-PO(R^{13})(R^{14})$, (where R^{13} and R^{14} are independently alkyl, aryl, alkoxy, aryloxy, heteroaryl, heteroarylalkyl, heteroaryloxy, heteroarylalkoxy, cycloheteroalkyl, cycloheteroalkylalkyl, cycloheteroalkoxy, or cycloheteroalkylalkoxy); and may be optionally independently substituted with from one to five substituents, which may be the same or different;

including pharmaceutically acceptable salts thereof, prodrugs thereof, and all stereoisomers thereof[; with the proviso that where Z is imidazole-4-yl, 5-alkylimidazol-4-yl or 5-cyclohexylimidazol-4-yl, then R^1 cannot be benzoxazole, benzthiazole, benzimidazole or pyridine].--

--71. (Amended) The compound as defined in Claim 64 wherein R^1 is